ORIGINAL ARTICLE

Responsible Use of Oral Corticosteroids in People with Comorbid Diabetes: An Expert Consensus

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Abstract

Globally, diabetes mellitus (DM) is a substantial contributor to morbidity and mortality. Comorbidities and intercurrent illnesses in people with diabetes may necessitate the use of steroids. Acute as well as chronic use of steroids contributes substantially to the development of various complications. Despite this, there are no standard guidelines or consensus to provide a unified approach for the rational use of steroids in people with diabetes. Also, there is scant harmonization among clinicians with the use of different steroids in routine practice. To address the inconsistencies in this clinical arena, the consensus working group (CWG) formulated a unified consensus for steroid use in people with diabetes. In people with diabetes, the use of steroids causes hyperglycemia and may precipitate diabetic ketoacidosis (DKA). An increase in weight is directly related to the dose and duration of the steroid therapy. Steroid-related alterations in hyperglycemia, dyslipidemia, and hypertension (HTN) add to the increased risk of cardiovascular (CV) disease. The risk of complications such as infections, osteoporosis, myopathy, acne, cataracts, and glaucoma may increase with the use of steroids. Appropriate and timely monitoring of these complications is necessary for early detection and treatment of such complications. Given the systemic effects of various antihyperglycemic drugs, there is a possibility of aggravating or diminishing the specific complications. Preference to a safer steroid is required matching the steroid dose equivalence and individualizing patient management. In conclusion, short-, intermediate-, or long-term use of steroids in people with diabetes demands their rational use and holistic approach to identify, monitor, and treat the complications induced or aggravated by the steroids.

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Introduction

Among the noncommunicable diseases (NCD), diabetes mellitus (DM) is a major NCD affecting the global population. The International Diabetes Federation (IDF) estimates India as the second highest prevalent country for DM. The disease unawareness is substantial with one out of two adults living with DM being unaware of the disease.[1] A recent ICMR-INDIAB-17 study identified 11.4 and 15.3% prevalence of diabetes and prediabetes, respectively. Prevalence also significantly varies in different regions in India. Projections suggest that currently, 101.3 and 136 million are suffering from diabetes to prediabetes, respectively.[2] Hypertension (HTN) is the most prevalent comorbid condition in people with diabetes. ICMR-INDIAB study projected over 315 million people with HTN in India.[2] People with diabetes have an increased likelihood of certain comorbid conditions or may develop intercurrent illness that requires treatment with short-, intermediate-, or long-term use of corticosteroids.[3–9] Such use of steroids in people with diabetes can increase the risk of various complications.[10,11] As no specific guidelines or consensus are addressing the issue of appropriate use of steroids in preexisting diabetes, the consensus working group (CWG) provides the Indian expert consensus for the rational use of oral steroids in people with diabetes.

Materials and Methods

In this consensus development, the CWG used the nominal group technique. This technique allows for the direct interaction of the experts.[12] In the first CWG meeting, consensus topics were discussed to arrive at a specific conclusion on a given consensus. Various topics included challenges with the use of steroids in people with diabetes, monitoring and management of different complications, considerations about the use of antihyperglycemic drugs, drug–drug interactions, and the concept of steroid equivalence. Based on the discussions in the first CWG meeting, evidence related to the chosen consensus topics was discussed in detail and a manuscript with draft consensus statements was prepared. In a subsequent working group meeting, further discussions on evidence led to the finalization of consensus statements. After approval of the final manuscript draft from all the experts, it was submitted for publication.

Diabetes and Corticosteroids: a Double Whammy

In people with diabetes, the use of steroids is associated with an increased risk of various

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complications. In understanding the rates of complications, Caughey et al.[10] assessed 18,226 people with diabetes, of which 67.2% had received steroid treatment within the past year and 5.9% had chronic obstructive pulmonary disease (COPD). In this study, there was a 94% increased risk of hospitalization for diabetes-related complications and the risk persisted irrespective of the route of steroid administration, that is, inhaled, oral, or both. Another study reported an increased risk of diabetes progression and osteoporosis onset with the use of steroids among the COPD population.[13] The risk of new infections and infections-related hospitalizations are also significantly increased by the use of steroids in people with diabetes than those without diabetes.[14] These data highlight the need to consider the rationale use of steroids in people with diabetes. Table 1 highlights the various complications that can occur with the use of steroids in people with diabetes.

Endocrine and Metabolic Complications

Hyperglycemia and Diabetic Ketoacidosis

The use of steroids is associated with an increased risk of hyperglycemia.[15–19] Hyperglycemia can occur as early as 5–8 hours after oral steroids.[20] Figure 1 provides a schematic representation of mechanisms by which steroids cause increased glucose levels and ketonemia.[18,21–27] In the short-term, hyperglycemia is usually the result of hepatic gluconeogenesis, increased glucagon secretion, reduced uptake of glucose in peripheral tissues, reduced insulin sensitivity, and reduced adiponectin levels in adipose tissues. Increased appetite and leptin resistance are mediated through central mechanisms. With longer use of steroids, there may be reduced insulin secretion, progressive β-cell failure, and reduced muscle mass further accentuating hyperglycemia. Further, hyperglycemia, insulin deficiency, osmotic diuresis, and increased catabolism may precipitate diabetic ketoacidosis (DKA) in vulnerable patients. Multiple reports suggest a possible likelihood of DKA after the initiation of steroids in people with diabetes.[28–30] Early identification of steroid-induced hyperglycemia is essential to avoid progression to DKA.

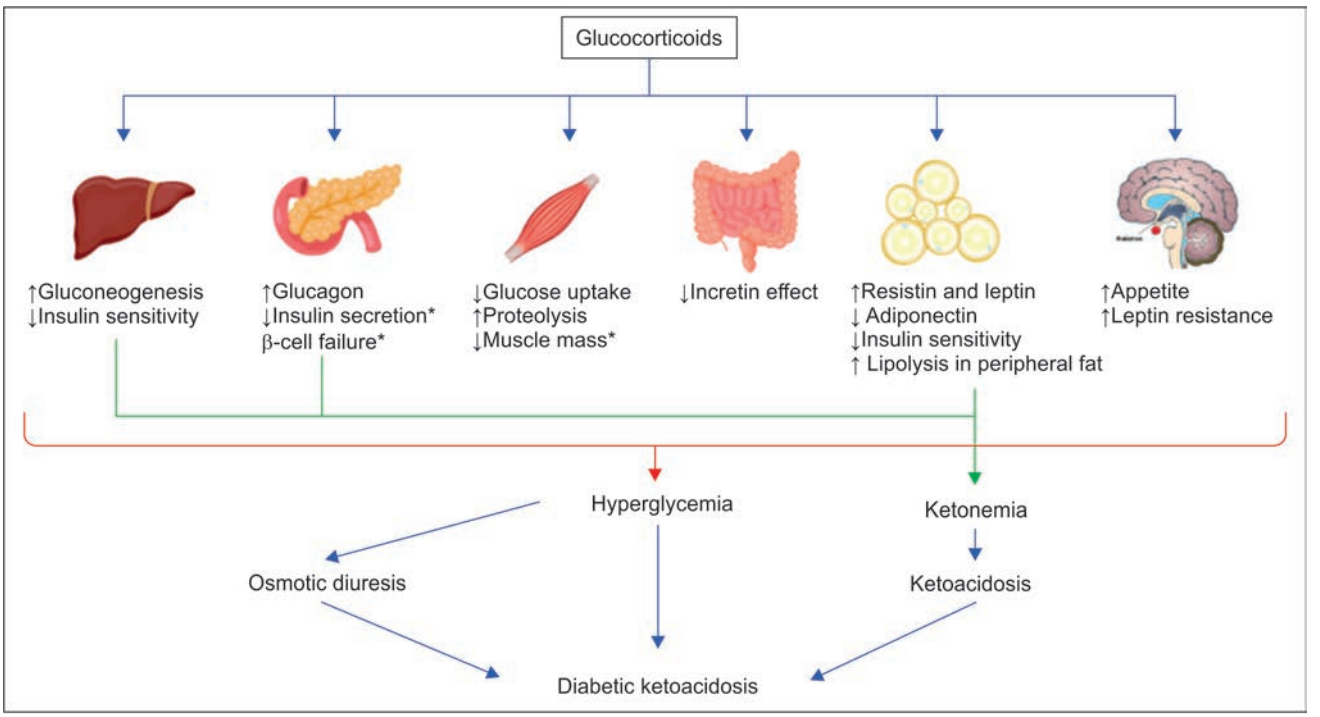
- **Expert consensus:** In people with diabetes, the use of steroids causes hyperglycemia and may precipitate DKA in vulnerable populations.

Weight Gain

Weight reduction of even 5% is known to improve glycemic control and reduce the need for antihyperglycemic medications. Such effects are mediated *via* improved insulin sensitivity and better β-cell function.[31] Chronic glucocorticoid therapy (>3 months) is associated with weight gain. Higher doses and previous exposure to glucocorticoids increase the risk of weight gain.[32] A year of steroid therapy can lead to a weight gain of >10 kg in nearly one-fifth of patients.[33] Such weight gain may further contribute to hyperglycemia and metabolic derangement in people with diabetes.

Table 1: "Double whammy" of DM and corticosteroid use

Endocrine and metabolic complications
• Hyperglycemia
• DKA
• Weight gain
• Hypothalamic–pituitary–adrenal axis suppression
CV complications
• HTN
• Dyslipidemia
• CVD
• HF
• Atrial fibrillation
Immunological complications
• Infections (bacterial, viral, fungal)
• Wound healing
• Acne
Musculoskeletal complications
• Myopathy
• Osteoporosis and bone fractures
• Avascular necrosis
Ophthalmological complications
• Cataract
• Glaucoma



*With prolonged use of glucocorticoids

Fig. 1: Mechanisms underlying glucocorticoid-induced hyperglycemia; *with prolonged use of glucocorticoids

- **Expert consensus:** In people with diabetes, weight gain is expected during steroid therapy and is directly related to the steroid dose and duration of the steroid therapy.

Hypothalamic–Pituitary–Adrenal Axis Suppression

Systemic use of steroids is known to impact the hypothalamic–pituitary–adrenal (HPA) functioning causing immediate and prolonged suppression in asymptomatic individuals.[34] In people with diabetes, there is diurnal variation and altered regulation of the HPA axis. Increased levels of basal adrenocorticotropic hormone (ACTH) and cortisol are seen. These increased levels of endogenous steroids hamper the glycemic levels and contribute to increased cardiovascular (CV) risk.[35,36] Clinically, suppression of the HPA axis may manifest as adrenal insufficiency (AI) or adrenal crisis and usually presents with nonspecific symptoms and signs (Table 2). Adrenal suppression can occur earlier than expected, especially with high doses of steroids. Sudden discontinuation of steroids also results in AI and, therefore, tapering of steroids is a common practice globally.[37] Thus, in people with diabetes, there may be a need for monitoring of AI.

- **Expert consensus:** In people with diabetes, AI can occur with discontinuation of steroids. AI is not related to the dose or duration of steroids.

Iatrogenic Cushing's disease, though uncommon, can occur and may go unnoticed causing disruptions in cardiometabolic features.[38,39] Risk factors include younger age, high basal body mass index (BMI), and higher calorie intake.[40] The incidence of cushingoid features is directly proportional to the steroid dose. Even at a small dose of <5 mg/day of prednisolone equivalent (PEQ), there is a 4.3% risk of iatrogenic Cushing's disease, and the risk increases to 15.8%, and 24.6% with a PEQ dose of 5–7.5 mg/day and >7.5 mg/day, respectively.[41]

- **Expert consensus:** In people with diabetes, iatrogenic Cushing's syndrome is a possibility that is directly proportional to steroid dose.

Table 2: Symptoms and signs indicative of possible AI

Excessive tiredness or fatigue
Insomnia
Palpitations
Brain fogging
Frequent dizziness
Hypotension

Cardiovascular Complications

Hypertension, Dyslipidemia, and Cardiovascular Disease

Hypertension in individuals with diabetes significantly increases the risk of CV events and mortality.[42] Steroids can induce HTN by affecting the water and electrolyte balance. However, other possible mechanisms involving vascular smooth muscles and nonvascular mechanisms also play a role in the causation of HTN.[43] A cumulative PEQ dose of ≥7.5 mg/day is associated with a 17% increased risk of HTN.[44] In people with diabetes, such steroid-induced HTN may further increase the CV risk.[43,45]

In Indians, diabetic dyslipidemia is characterized by high postprandial triglycerides (TGs), low high-density lipoprotein cholesterol (HDL-C), normal or increased low-density lipoprotein cholesterol (LDL-C), and substantial presence of small dense LDL-C particles.[46] Corticosteroids are reported to have dose-dependent effects on lipoprotein.[47] They trigger lipolysis, lipoprotein lipase activity, adipokine activity, inhibit fatty acid oxidation, and increase insulin resistance.[46,48] Therefore, dyslipidemia in people with diabetes may be precipitated by the concurrent use of steroids.

Diabetes is considered a coronary heart disease risk equivalent.[49,50] Dysglycemia, dyslipidemia, and HTN with steroid use contribute to increased CV risk. Chronic steroid use impacts the vascular endothelium and contributes to the accelerated atherosclerotic process and thereby CV disease (CVD).[51–53] This has been proven in various clinical studies. Pujades-Rodriguez et al.[52] identified that with the prescribed steroid dose in 87,794 persons with immune-mediated inflammatory disorders and no history of CVD at baseline, there was a significant dose-dependent increase in the risk of CVDs at a 5-year median follow-up, regardless of the disease activity level. CVD risk at a PEQ dose of <5 mg/day and up to 25 mg/day was studied. The 5-year cumulative risk for CVD increased from 7.1% in nonusers to 28% for PEQ dose of ≥25 mg/day. Figure 2 shows the risk of various CVDs with different doses of steroids.[52] It indicates even with the lowest dose of <5 mg/day PEQ, the risk of CV events is increased.

- **Expert consensus:** In people with diabetes, steroids may cause or exacerbate HTN and dyslipidemia. The risk of CVDs is increased even at a PEQ dose of <5 mg/day.

Heart Failure

In people with diabetes, there is diastolic dysfunction in the early stages that ultimately progresses to systolic dysfunction over a period if not intervened.[54] Heart failure (HF) with preserved ejection fractions (HFpEF) represents nearly 50% of HF cases.[55] Oral glucocorticoid use is independently associated with an elevated risk of HF. Even after adjustment for drugs such as antihyperlipidemic, antihypertensive, and oral antihyperglycemic agents, oral corticosteroid use is independently associated with an increased risk of CV events such as HF.[52] Thus, in people with diabetes and HF, steroids may precipitate HF. The mineralocorticoid activity of oral steroids also needs to be considered when using them, especially in patients with HTN and HF.

- **Expert consensus:** In people with diabetes, steroids may precipitate HF and thus consider the mineralocorticoid activity of steroids in such populations.

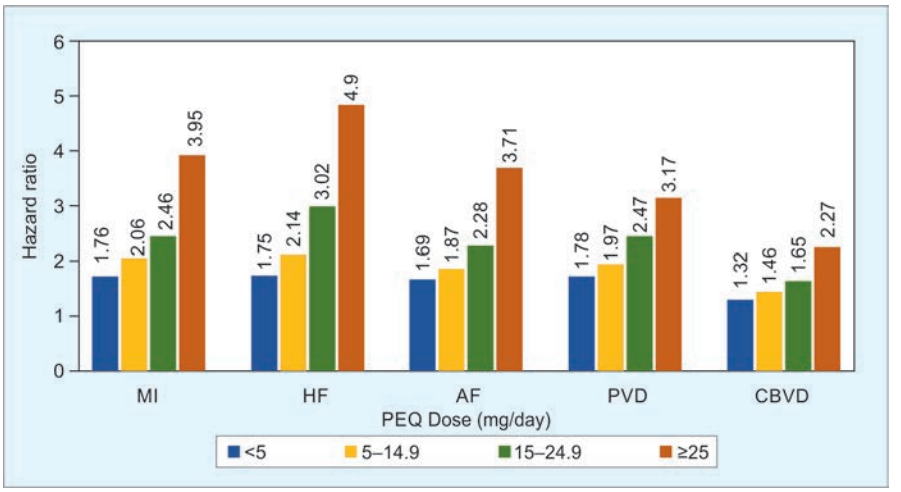


Fig. 2: Risk (hazard ratios) of different CVDs with different doses of steroids[52]; AF, atrial fibrillation; CBVD, cerebrovascular disease; HF, heart failure; MI, myocardial infarction; PEQ, prednisolone-equivalent; PVD, peripheral vascular disease

Immunological Complications

Infections

Diabetes compromises the functioning of neutrophils, the antioxidant system, and humoral immunity, and decreases the secretion of inflammatory cytokines.[56] The anti-inflammatory and immunosuppressive effects of steroids make them useful in various inflammatory and autoimmune disorders.[57] The Atherosclerosis Risk in Communities (ARIC) study on people with diabetes reported a significantly increased risk of hospitalizations and mortality related to infections.[56]

The suppression of the immune system and the worsening of preexisting diabetes by steroids further increases the risk of infection in people with diabetes. Conversely, infections in people with diabetes might result in other diabetic complications such as hypoglycemia and ketoacidosis.[58,59] The risk of infections increases proportionally with the dosage and duration of steroids. Elderly age and concurrent use of other immunosuppressive medications increase infection risk further. Due to the inhibition of cytokine release and the resulting decrease in inflammatory and febrile responses, patients using glucocorticoids may not exhibit typical signs and symptoms of infection (e.g., fever), making it difficult to diagnose infections early.[60] One important consideration is the risk of genital mycotic infections (GMIs) with the use of sodium-glucose cotransporter-2 inhibitors (SGLT2i). A study from the United Kingdom analyzed the data of nearly 21,000 patients and found no increased risk of GMIs with oral steroid use. However, the study may not be powered to detect a small increase in the risk of GMIs.[59] Thus, future research is necessary to understand whether steroids increase the risk of GMIs in people with diabetes receiving SGLT2i.

- **Expert consensus:** In people with diabetes, steroids may increase the risk of bacterial, viral, and fungal infections. Classical features of infections may not be evident in some of the patient populations. Further research is necessary to understand the risk of infections in such populations.

The risk of drug interactions is an important consideration when using appropriate antimicrobials (Table 3).[61,62] The use of CYP3A inhibitors concomitantly with steroids likely increases the risk of systemic side effects. For example, antifungals such as ketoconazole, antibiotics like clarithromycin, and antivirals like ritonavir can increase the systemic exposure of steroids and cause toxicity. On the other hand, rifampin can reduce steroid exposure and reduce its efficacy. Therefore, monitoring of patients for possible toxicity signs of steroid overdosage is necessary and dose alteration may be needed in some patients taking such concurrent medications.

- **Expert consensus:** In people with diabetes, steroids may have drug interactions with some antimicrobials and other medications. A watch for systemic toxicity of steroids is necessary with the concomitant use of certain medications.

Wound Healing

Uncontrolled DM impairs wound healing. Concurrent long-term use of steroids in people with diabetes hampers wound healing. In one study, the postoperative use of steroids for over 30 days was associated with a 4-fold higher mortality, a 2–3-fold increase in wound dehiscence, and a 5% increase in infection rates.[61]

- **Expert consensus:** In people with diabetes, steroids might delay wound healing. Caution is necessary in people with diabetes with preexisting foot ulcers.

Acne

Acne flares can be seen with the use of steroids in people with diabetes. Risk factors for steroid acne include the following:

- Higher steroid dosage.
- Application of steroid with occluded patch.
- Young age (<30 years).
- Previous history of acne.

There may be a faster progression of acne and the formation of hyperkeratosis, microcomedone production, papular–pustular lesions, and follicle ruptures.[63]

- **Expert consensus:** In people with diabetes, steroids may increase the occurrence of acne, especially with higher dosage and in the presence of risk factors.

Musculoskeletal Complications

Myopathy

Skeletal muscles are an important part of the "ominous octet" essential to the regulation of blood glucose. Diabetes-related myopathy is characterized by a failure to maintain adequate functioning of muscles. Diabetes affects the muscle progenitor cell population and impairs mitochondrial functioning which is critical in maintaining skeletal muscle health.[64] Compared to nondiabetics, there is a 1.5 times greater risk of sarcopenia in people with diabetes.[65,66] In the Indian population, sarcopenia is seen in nearly 17% of people with diabetes.[67] The use of steroids in people with diabetes may further cause muscle damage because of its direct catabolic effects. Muscle damage associated with steroid use can occur after weeks to months and may appear early with higher dosages.[60]

- **Expert consensus:** In people with diabetes, steroids may increase the risk of myopathy and it may occur early in the course with a higher dosage of steroids.

Osteoporosis and Bone Fractures

Evidence suggests that one in three women and one in five men aged over 50 years will sustain an osteoporotic fracture.[68] Both DM and osteoporosis can coexist, especially in the elderly, and are impacted by aging and lifestyle changes. There is a direct relationship between type 2 diabetes mellitus (T2DM) and bone strength.[69] In people with diabetes, advanced glycation end-product accumulation, changes in collagen cross-linking, and suppression of bone turnover are the main factors affecting bone strength.[70] T2DM alone is a significant risk factor for major osteoporotic fractures (MOFs) such as low trauma hip fractures, and fractures at the proximal humerus, clinical spine, and distal radius. The risk is regardless of bone mineral density (BMD) and BMI. T2DM raises the risk of a fracture by at least 20–30%. Such an increase in risk is comparable to rheumatoid arthritis or a familial hip fracture.[69]

Glucocorticoid-induced osteoporosis (GCOP) is usually an iatrogenic osteoporosis and is a frequently observed cause of osteoporosis. Nearly, 30–50% of patients on chronic glucocorticoid therapy may get

Table 3: Drug interactions of steroids

Drug groups	*Interaction*
Antivirals (e.g., ritonavir, indinavir), ciclosporin Antifungals (e.g., ketoconazole, itraconazole) Macrolides (e.g., erythromycin, clarithromycin)	Inhibit metabolism ↑ Systemic steroid exposure
Rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, ephedrine, and aminoglutethimide	Increased metabolism ↓ Steroid systemic exposure and effect
Anticoagulants (e.g., warfarin), aspirin, other nonsteroidal anti-inflammatory drugs	↑ Gastrointestinal bleeding
Diuretics (e.g., furosemide, hydrochlorothiazide)	↑ Hypokalemia
Methotrexate	Hematological toxicity

fractures. Long-term oral steroid therapy increases fracture risk. Fractures may occur at a lower threshold of BMD.[71] PEQ dose of >5 mg daily leads to a reduction in the BMD with a rapid increase in fracture risk within 3–6 months of starting steroid therapy. The risk of fractures is independent of underlying disease, age, and gender.[72] Thus, combined with diabetes, the risk of bone loss and fractures may get substantially elevated with concomitant steroid therapy.

- **Expert consensus:** In people with diabetes, steroids increase the risk of osteoporosis even at a PEQ dose of 5 mg or more. Duration of steroids is associated with such risk of osteoporosis and related bone fractures.

Avascular Necrosis

In people with diabetes, the risk of avascular necrosis may be increased slightly. A meta-analysis of six observational studies reported a nonsignificant increase in the risk of avascular necrosis at sites other than the jaw.[73] The use of steroids is one of the most common causes of iatrogenic avascular necrosis of various bones and joints. The prevalence of steroid-induced avascular necrosis ranges between 3 and 38%. Though femoral and humoral heads are the most common sites, avascular necrosis can occur in other bones such as knee joints, foot bones, ankles, and hands. A positive correlation with a steroid dose of ≥40 mg/day of PEQ dose is reported.[74] Exposure to bolus doses increases the risk of avascular necrosis substantially.[74,75] A study in Taiwan identified a 16% greater risk of avascular necrosis of the femoral head in people with diabetes compared to those without diabetes. Also, a 34% increased risk of avascular necrosis of the femoral head with oral steroid use was reported.[76]

- **Expert consensus:** In people with diabetes, steroids may increase the occurrence of avascular necrosis of the femur and the risk is probably higher with a higher dose of steroids.

Ophthalmological Complications

Cataract

The risk of cataracts in people with diabetes is five times higher than in nondiabetics. It commonly produces cortical and/or posterior subcapsular cataracts.[77] Prolonged use of steroids increases the risk of posterior subcapsular cataracts and nuclear cataracts.[78] A study reported that intravitreal use of triamcinolone for diabetic macular edema over 3 years led to a significantly higher proportion of cataract extractions compared to sham-treated eyes (56 vs 8%, $p < 0.0001$).[79] In another study assessing a population with diabetic retinopathy, the concomitant use of systemic steroids led to an increased risk of sight-threatening cataracts.[80] Thus, in people with diabetes, long-term use of systemic steroids accelerates cataract formation.

- **Expert consensus:** In people with diabetes, steroids increase the risk of cataracts and the risk increases with the duration of their use.

Glaucoma

The risk of glaucoma is significantly higher in people with diabetes. A meta-analysis of seven prospective studies identified a risk ratio of 1.36 (95% CI 1.24–1.50) for primary open-angle glaucoma (POAG).[81] It is well established that the use of steroids is associated with increased intraocular pressure (IOP) leading to glaucoma.[82]

- **Expert consensus:** In people with diabetes, steroids may increase the risk of glaucoma.

Monitoring for Complications during Steroid Therapy

As discussed in previous sections, the "double-whammy" of diabetes and corticosteroid use leads to complications that affect the overall health of an individual. Monitoring for these complications can be useful to detect them early and treat them adequately. Table 4 provides the schedule of monitoring of different functions in people with diabetes receiving steroids.[60]

Glycemia Monitoring

Postprandial hyperglycemia is the first observable dysglycemia response with the use of short- or intermediate-acting steroids such as prednisolone. The effect on glucose levels can be evident within a few hours to days after initiating steroids.[83] Therefore, it is advised to screen blood glucose levels for frequent intervals in the first few days of starting treatment. The Canadian guidelines advocate monitoring of glycemic parameters for at least 48 hours after initiation of steroids.[84] The frequency of monitoring in the long run is not fixed. Higher baseline glycated hemoglobin (HbA1c) is associated with a greater increase in glucose after steroid initiation.[85] Thus, monitoring should be individualized according to baseline glycemic status, number of medications, age, DKA risk, etc. There are intraday variations in blood glucose levels among patients with steroid-induced hyperglycemia. people with diabetes may have glucose levels above the target range for at least 6 hours daily with over 1 hour of severe hyperglycemia.[86] Longer duration above the normal glycemic target shows that the glycemic variability may be greater in people with diabetes receiving steroids. Thus, there may be a need for continuous glucose monitoring (CGM) in some cases. CGM is an established modality for both type 1 and type 2 diabetes especially for those who are receiving insulin. CGM can provide better treatment guidance and personalized diabetes care.[87] In the Indian context, CGM is useful in patients with diabetes and should be offered to those who can afford it. For patients on insulin, the use of CGM with time-in-range (TIR) metric may be done for at least 2 weeks to adjust the antihyperglycemic drugs. Patients with a frequent hypoglycemia history get more benefits from CGM.[88] CGM can help understand the glycemic fluctuations after steroid initiation and guide the therapy for steroid-induced hyperglycemia. However, physicians need to be cautious while assessing the TIR metric in such situations. For optimization of decision-making, CGM-TIR can be combined with self-monitoring of blood glucose.

- **Expert consensus:** In people with diabetes, specific monitoring approaches are essential for early detection and treatment of various complications.

Management Considerations

The complications and difficulties arising out of steroid use in comorbid diabetes can be complex and difficult to manage. Despite their occurrences, we need to continue the antihyperglycemic treatments to provide optimal glucose control. This can be done by assessing the benefit–risk balance with antihyperglycemic medications. Table 5 prompts the possible risks and benefits of currently available antihyperglycemic drugs.[89–102] This can help make individualized treatment changes in the routine management of people with diabetes using steroids.

Hyperglycemia

In India, the Research Society for Study of Diabetes in India (RSSDI) 2022 guidelines provide effective management strategies for treating steroid-induced hyperglycemia.[103] It is advised to review the current treatments and modify them to achieve mean blood glucose control in the range of 106–180 mg/dL. However, the goals need to be set by considering the individual characteristics, comorbidities, compliance, and risk of hypoglycemia. Table 6 provides various glycemic goals for patients developing steroid-induced hyperglycemia in specific scenarios.

Steroid-induced hyperglycemia should be persuaded with care. Depending on the severity

Table 4: Monitoring of different complications in people with diabetes initiating long-term steroid

Endocrine and metabolic monitoring	*Monitoring actions*
Baseline assessments	Anthropometry: Height, weight, BMI Glycemic: FBG, PPBG, and HbA1c Ophthalmic: Vision, intraocular pressure Other: Blood pressure, complete blood count
Glycemia monitoring	Individualized based on: Baseline glycemic status Number of medications Age DKA risk More frequent in the 1st week of steroid therapy CGM If available, may be considered in patients receiving or requiring insulin CGM can be taken for at least 2 weeks with special consideration of TIR CGM with SMBG provides a better understanding of glycemic changes
Adrenal insufficiency	Only in suspected cases Monitor morning (8 AM) serum cortisol levels (e.g., every 12 weeks). Levels <3 µg/dL (80 nmol/L) suggest AI If AI is strongly suspected with normal cortisol levels, perform low dose ACTH stimulation test After 1 µg of cosyntropin, peak cortisol <18 µg/dL (<500 nmol/L) at 0, 30, 60 minutes: diagnosis of AI
CV monitoring	
Lipids profile	After 1 month and then every 6–12 months More frequent in patients with existing dyslipidemia
CVD	Individualized assessment
Musculoskeletal monitoring	
Myopathy	Screen for symptoms and signs related to muscle damage in every clinical visit Educate patients about muscle pains or aches Perform tests of muscle strength (such as hand grip strength, etc.) at regular intervals to assess myopathy
Bone health	Children BMD at 3 months after starting steroid If normal, reassess every year More frequent in patients with cushingoid features, vertebral growth deceleration, and fractures after mild trauma Adults BMD at 1 year after starting steroids If normal, reassess every 2–3 years Frequent assessment in obese, frail, and physically inactive patients
Height/weight velocity	Assess the height of children annually and plot the growth curve (e.g., every 6 months) Use IAP growth charts for height/weight velocity monitoring
Avascular necrosis	Screen for bone or joint pain radiating to nearby areas that are likely avascular necrosis MRI, if strong clinical suspicion
Ophthalmic monitoring	
Cataract	Assess at baseline before starting steroids Reassess every 3–6 months Frequent assessment in elderly (>60 years)
Glaucoma	Assess IOP at baseline Reassess annually Frequent IOP measurement Family history of glaucoma High myopia cases Comorbid connective tissue disorders

BMD, bone mineral density; CGM, continuous glucose monitoring; IAP, Indian Academy of Pediatrics; IOP, intraocular pressure

Table 5: Antihyperglycemic agents benefits and risks in view of steroid use in comorbid diabetes[89–102]

Complications	*Metformin*	*SUs*	*TZDs*	*DPP4i*	*SGLT2i*	*GLP-1 RAs*	*AGIs*
Hyperglycemia	B	B	B	B	B	B	B
DKA	–	–	–	–	R	–	–
Weight gain	B/NR	R*	R	NR	B	B	NR
HTN	NR	U	U	NR	B	B	NR
Dyslipidemia	NR	U	B	NR	U	U	U
HF	U	U	R	R/NR[!]	B	U	U
Bone fractures	U	U	R	NR	R/NR[#]	U	U

*Glimepiride and gliclazide modified release do not increase weight; !saxagliptin and alogliptin worsen heart failure and sitagliptin and linagliptin do not increase HF events; [#]canagliflozin increased fracture risk whereas dapagliflozin and empagliflozin do not increase fracture risk; B, beneficial; NR, not risky; R, risky; U, unclear

Table 6: Research Society for Study of Diabetes in India 2022 glycemic goals for subjects with diabetes developing steroid-related hyperglycemia[103]

Population	*Glycemic goals (mean glucose level)*
Hospitalized patients	140–180 mg/dL
Frailty	120–200 mg/dL (round the clock)
Care home residents	126–216 mg/dL

Table 7: Preferred antihyperglycemic by the type of steroid

Steroid	*Preferred antihyperglycemic drugs*	*Insulin dose[#]*
Short-acting (e.g., hydrocortisone)	SU* ± short-acting insulin[!]	Initiate at 0.01 IU/kg Intensify based on pre-prandial glucose: 200–300 mg/dL: 0.04 IU/kg >300 mg/dL: 0.08 IU/kg
Intermediate-acting (e.g., prednisolone)	SU* ± NPH insulin[!]	Initiate at 0.4 IU/kg
Long-acting (e.g., dexamethasone)	SU* ± NPH + short-acting insulin, OR long-acting insulin (e.g., insulin glargine)!	NPH/detemir twice daily: Initiate at 0.3 IU/kg Glargine/degludec once daily: Initiate at 0.2 IU/kg

*Gliclazide may be preferred over other sulfonylureas if it is not included in the current management algorithm of the index patient; [#]when used to manage steroid-induced hyperglycemia; !as necessary (for e.g., use NPH insulin twice daily if steroid is used two times a day)

of hyperglycemia and the pharmacodynamic action of steroids, existing antihyperglycemic drug modifications and/or the addition of newer agents can be considered. We recommend "escalation" and "de-escalation" approaches (Fig. 3). Figure 4 provides a broad schematic treatment approach for type 1 and type 2 diabetes. Table 7 lists the possible antihyperglycemic medications according to the type and timing of steroid administration.[103] One must consider the insulin of choice based on insulin(s) pharmacokinetics that match with pharmacodynamic impact of specific steroids on glycemic excursions.[60] A series of four cases reported good efficacy of exenatide in improving the glycemic levels in such patients.[104] Figure 5 provides a glycemic profile after the use of different duration steroids and likely useful insulin according to such profile. As recommended by the RSSDI guidelines, a correction factor is necessary when the use of insulin is necessary. A correction factor is equal to 1800 divided by the total daily dose if insulin analog is used or 1500 divided by the total daily dose if regular insulin is used.[103] Detailed dosing recommendations on insulin use are out of the scope of this paper. Clinicians should follow the local recommendations for determining insulin doses and appropriate titration of insulins.

In the escalation approach, modify the doses of existing antihyperglycemic drugs as per the severity of steroid-induced hyperglycemia. For the use of additional antihyperglycemic drugs, consider guidelines-directed management of hyperglycemia. In the de-escalation approach,

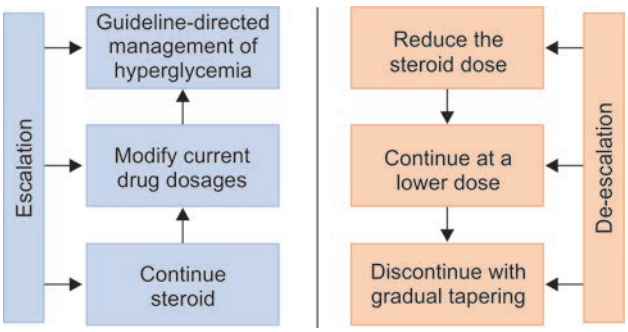


Fig. 3: Escalation and de-escalation approach for the use of steroids in people with comorbid diabetes

reduce the steroid dose and continue at a lower dose to understand the glycemic response. If persistently raised glucose levels are seen, consider discontinuation of steroids with gradual tapering.

Diabetic Ketoacidosis

Diabetic ketoacidosis should be managed in the intensive care unit as per the standard DKA treatment protocol involving fluids, insulin, and electrolyte treatment. For patients who develop DKA, it is advisable to reduce the dosages or stop steroids if possible.

Weight Gain

Adequate nutrition and exercise, till the steroids are continued, can help prevent weight gain. The current evidence from randomized trials is very limited. Studies in children with lupus, and hematological malignancies have shown that a low-calorie diet and home-based exercises helped to promote weight loss over 6 weeks to 1 year.[105–107] However, there is a need to generate further evidence as to which dietary and exercise interventions would best fit to contain weight gain with the use of steroids.[107] As people with diabetes need to follow aggressive lifestyle interventions, weight gain with steroid use may be expected to be lower. However, it needs to be studied further in prospective trials. Based on the current evidence, one can prefer the medications that promote weight loss in diabetes. SGLT2i and glucagon-like peptide 1 receptor agonists (GLP-1RA) help promote

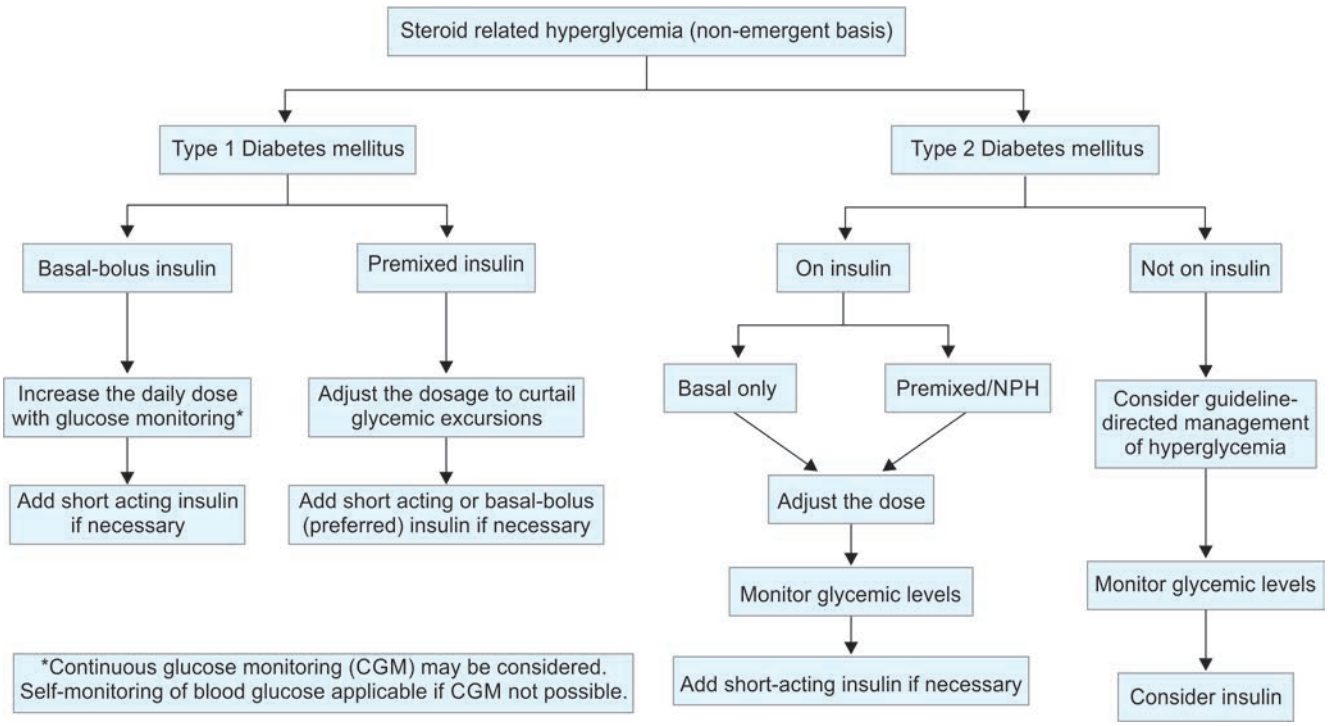


Fig. 4: Treatment approach to steroid-induced hyperglycemia in people with comorbid diabetes proposed by CWG

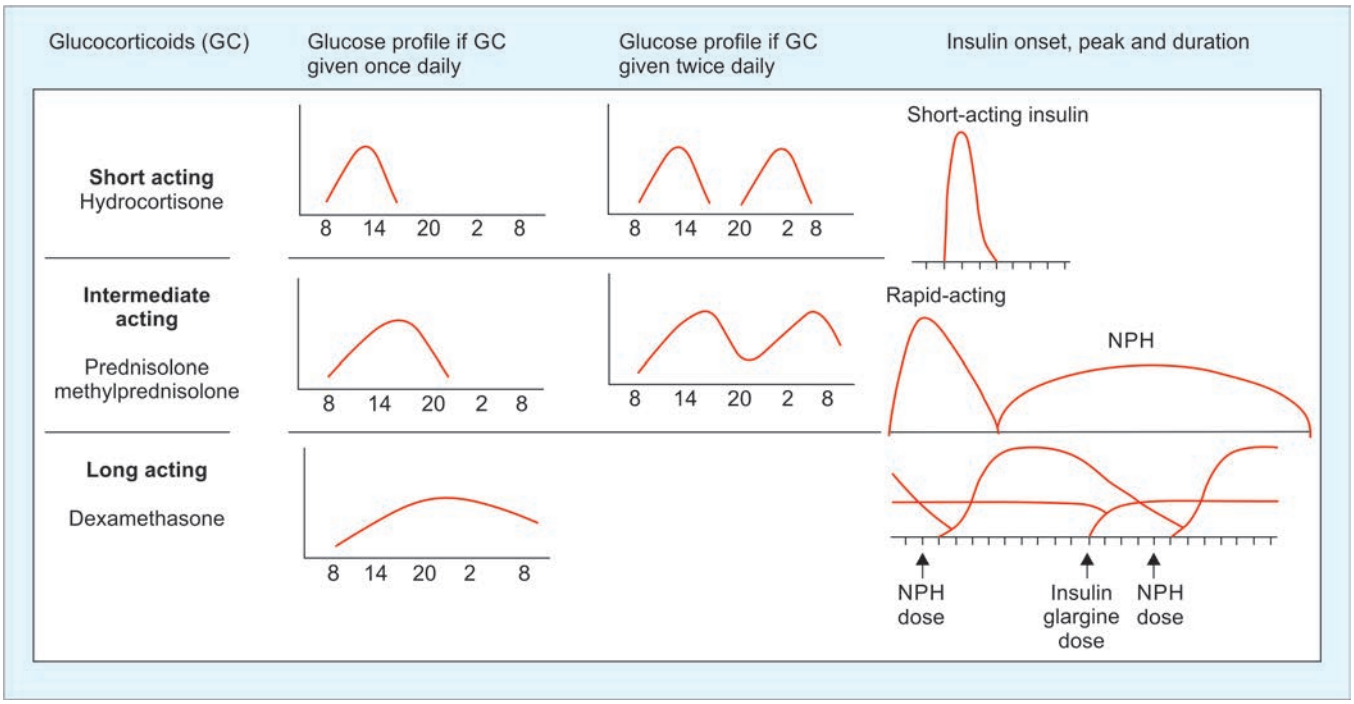


Fig. 5: Representative profile of hyperglycemic effect from steroids to matching profile of different insulins

weight loss in people with diabetes.[108] These agents can be preferred over other medications for patients using steroids who are at a greater risk of weight gain. However, it is notable to mention here that SGLT2i use carries a risk of DKA in insulinopenic patients.

Heart Failure

Among the antihyperglycemic drugs, SGLT2i and GLP-1RA have proven benefits in CVD protection.[109,110] The dipeptidyl peptidase-4 inhibitors (DPP4i) (e.g., sitagliptin, linagliptin) have shown CV safety. Saxagliptin and alogliptin have shown worsened HF outcomes.[111] Therefore, in cases where CVD risk is estimated to be higher, preference for individual classes of drugs should be considered. When using these medications, one needs to understand possible side effects. SGLT2i as a group may precipitate DKA, especially in insulinopenic patients.[112] Reports indicate the precipitation of DKA in a patient with diabetes treated with dexamethasone.[113] For HF, SGLT2i are first-line drugs whereas saxagliptin, alogliptin, and pioglitazone need to be avoided in HF patients.[114,115]

Infections and Wound Healing

Stricter glycemic control, appropriate antibiotic cover, and adequate local wound

care are necessary to improve wound healing.

Acne

Acne may disappear after 2–6 weeks of stopping steroids.[116] For the treatment of acne, a referral to a dermatologist should be sought.

Myopathy

Tests for muscle strength and quantitative tests to observe muscle loss can help diagnose myopathy. Besides glycemic control and reduction in steroid dose, aerobic and resistance exercises are recommended.[66] The protein intake is strongly related to skeletal muscle mass in older T2D patients. Essential amino acid supplementation helps improve muscle loss and increase muscle strength.[117–119]

Osteoporosis

In patients who are at risk of bone loss, therapeutic considerations are essential. Vigorous walking combined with weight-bearing activity and moderate-intensity aerobic exercise are advised. Supplement steroid therapy with a Mediterranean-style diet, omega-3 fatty acids calcium, and vitamin D with monitoring of bone health to prevent osteoporosis and subsequent fracture risk. Bisphosphonates, teriparatide, and denosumab may be considered with substantial bone loss.[71]

Another important aspect is antihyperglycemic therapy. Thiazolidinedione independently increases the risk of osteoporosis and fractures.[120,121] However, metformin, sitagliptin, and other DPP4i are neutral with effect on bone.[122–124] Among SGLT2i, a meta-analysis finds no significant increase in the risk of fractures in comparison to placebo.[125] However, canagliflozin increases the risk of fractures. Incretin-based therapies are safer concerning the effect on bone.[124]

Avascular Necrosis

Complaints of hip pain being referred to buttock, thigh, or knee, and shoulder pain radiating around the axilla can be early signs of avascular necrosis in the hip or humerus. Avoiding high bolus doses can be one preventive strategy. Stopping the steroid, if possible, should be done.

Glaucoma

Thus, monitoring of IOP is necessary in all patients with DM taking systemic steroids. With discontinuation of steroids, IOP may regress to normal levels within 4 weeks. However, in nearly 3% of cases, the response may be irreversible.[126] A timely referral to an ophthalmologist should be considered.

- **Expert consensus:** The complexity brought on by steroids in people with diabetes is enormous and clinical decisions in patient management should be individualized.

Steroid Equivalence Concept

Steroids are one of the most widely prescribed drugs globally and indications for their use are multifold. They differ in their relative anti-inflammatory and mineralocorticoid activities. The drug potencies of different steroids are indicated by their equivalent doses. The doses of different steroids are expressed as "prednisone equivalent" which means the dose of other steroids is as equally potent as the prednisolone dose.[127] Table 8 provides the dose equivalent potencies of different corticosteroids.[89,90,128,129] Dose-to-dose conversion should consider the equivalent dose of different steroids. In defining the conventional dosing with different corticosteroids, one should consider following the dose approach.

- Low dose: ≤7.5 mg/day PEQ.
- Medium dose: >7.5 to ≤30 mg/day PEQ.
- High dose: >30 to ≤100 mg/day PEQ.
- Very high dose: >100 mg/day PEQ.
- **Expert consensus:** The "steroid equivalence" should be considered in routine clinical practice appropriately to avoid underdosing or overdosing when shifting from one steroid to another steroid.

Among the intermediately acting steroids, deflazacort (DFZ) is one effective and safe steroid that is used widely for various indications (Table 9). DFZ is an oxazoline derivative of prednisolone. After intake, DFZ is converted to an active metabolite DFZ-2l-hydroxide. The oral bioavailability of DFZ is nearly 68%. It is metabolized in the liver and is excreted *via* urinary (~2/3rd) and fecal (~1/3rd) routes.[12] DFZ has been studied in various indications in comparison to prednisolone and methylprednisolone (MP). Below is brief evidence from select clinical studies that bring the comparative efficacy and safety of DFZ and establish the concept of steroid equivalence.

Steroid Equivalence: Clinical Evidence

Clinical studies have identified the steroid equivalence and established the efficacy and safety of different steroids (Table 10).[133–138] In a South Indian study involving 70 adult cases of active systemic lupus erythematosus (SLE) defined by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score of ≥3, 35 each were treated with 1.2 mg/kg/day of DFZ or 1 mg/kg/day of prednisone (PDN). Dose tapering was done every 3 weeks over 3–6 months. The efficacy of DFZ was similar to PDN at 3 and 6 months based on changes in SLEDAI score, renal SLEDAI, anti-double stranded deoxyribonucleic acid (anti-dsDNA) titers, and C3 and C4 levels. However, at 6 months, safety parameters revealed that DFZ was safer than PDN in terms of absolute percent increment in Cushing's severity index (100 vs 200%), body weight (3.3 vs 8.4%), and hirsutism score (11 vs 33%). Overall, the total number of serious adverse effects was also significantly lower with DFZ (4.8 vs 9.4%). Effect on the fasting blood glucose (FBG)

Table 8: Dose to dose steroid equivalence of different corticosteroids

Steroids	*Equivalent glucocorticoid dose*	*Anti-inflammatory potency relative to hydrocortisone*	*Mineralocorticoid activity relative to hydrocortisone*
Short acting (biological $t_{1/2}$ <12 hours)			
Hydrocortisone	20 mg	1	1
Intermediate acting (biological $t_{1/2}$ 12–36 hours)			
Prednisolone	5 mg	4	0.8
Methylprednisolone	4 mg	5	0.5
Deflazacort	6 mg	3–4	0
Long acting (biological $t_{1/2}$ >36 hours)			
Dexamethasone	0.75 mg	30	0

For example, a 20 mg dose of hydrocortisone is glucocorticoid equivalent to 5 mg of prednisolone. Also, 5 mg prednisolone is equivalent to 4 mg of oral MP and 6 mg of DFZ. This means that an individual receiving 20 mg of PDN needs to be shifted to 24 mg of DFZ for similar efficacy

Table 9: Approved indications of DFZ from the United States, United Kingdom, and India

Regulatory authority (approval year)	*Approved indications*
United States (2017)[130]	Duchenne muscular dystrophy (DMD) in patients aged ≥5 years
United Kingdom (1994)[131]	• Anaphylaxis, asthma, severe hypersensitivity reactions • Rheumatoid arthritis, juvenile chronic arthritis, polymyalgia rheumatica • SLE, dermatomyositis, mixed connective tissue disease (other than systemic sclerosis), polyarteritis nodosa, sarcoidosis • Pemphigus, bullous pemphigoid, pyoderma gangrenosum • Minimal change nephrotic syndrome, acute interstitial nephritis • Rheumatic carditis • Ulcerative colitis, Crohn's disease • Uveitis, optic neuritis • Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura • Acute and lymphatic leukemia, malignant lymphoma, multiple myeloma • Immune suppression in transplantation
India (2004)[132]	Asthma, rheumatoid arthritis

Table 10: Efficacy and safety of DFZ to other steroids in steroid equivalent dose

Authors (year)	*Study design*	*Population*	*Groups*	*Efficacy results*	*Safety results*
Ganapati et al. (2018)[133]	Prospective, observational	SLE: Adults ≥18 years, SLEDAI ≥3	DFZ (n = 35) vs PDN (n = 35)	Assessment at 3 and 6 months No differences in: SLEDAI score Renal SLEDAI Serum dsDNA Serum C3 and C4 levels No differences in remission rates at 3 (51.6 vs 58.6%) and 6 (77.4 vs 86.2%) months	At 6 months Weight increase: 3.3 vs 8.4% (p = 0.001) Hirsutism score change: 11 vs 33% (p = 0.002) Cushing severity index change: 100 vs 200% (p = 0.03) Absolute change in: FPG: −5 vs +9 mg/dL TC: −12 vs +17 mg/dL LDL-C: −7 vs +10.5 mg/dL BMD LS: Overall AEs: 4.8 vs 9.4% (p < 0.05) Infection requiring hospitalization: 2 vs 0
Singhal et al. (2015)[134]	Randomized, prospective	Idiopathic nephrotic syndrome children (2–12 years)	DFZ (n = 12) vs PDN (n = 13)	Remission rates: 12 (100.0%) vs 11 (84.6%), p = 0.480 Time to induce remission: 10.25 ± 2.41 vs 12.55 ± 1.44 days, p = 0.012 Relapse: 1 (9.1%) vs 3 (27.3%), p = 0.586	Height change: 2.13 ± 0.50 vs 1.44 ± 0.45 cm, (p = 0.0030 Weight gain: 1.36 ± 0.96 vs 1.38 ± 0.56 kg (p = 0.950)
Lippuner et al. (1998)[135]	Randomized, double-blind	Renal transplantation	DFZ (n = 8) vs PDN (n = 11)	78-week f/u Rejection: 2 vs 3 No difference in: Serum creatinine Ionized calcium ALP Urinary deoxypyridinoline	At 78 weeks BMD Lumbar: Reduced significantly in PDN not in DFZ group (p < 0.05 intergroup) Upper femur: Significant reduction in both groups Whole body: Decreased significantly in PDN but not in DFZ group Body weight: 1.8 ± 1 (p = 0.180) vs 3.8 ± 2 (p < 0.05) kg Lean body mass: Decreased significantly in both groups Fat mass: 3.5 ± 1.4 vs 7.1 ± 1.8 Significant increase in TC (p < 0.03), LDL-C (p < 0.01), and LpB2 (p < 0.03) with PDN in comparison to DFZ TG: Increased in PDN and decreased in DFZ group No significant differences in HbA1c change

Contd…

Contd…

Authors (year)	*Study design*	*Population*	*Groups*	*Efficacy results*	*Safety results*
Kim et al. (1997)[136]	Randomized, prospective	Renal transplantation with either pre-Tx DM or post-Tx DM	Conversion from PDN to DFZ (conversion group, *n* = 42) vs continuation of PDN (control group, *n* = 40)	Mean follow-up: 13.2 months No significant difference in two groups for serum creatinine, required cyclosporin A dose No significant change graft function or acute rejection after conversion	Significant reduction HbA1c from pre-Tx to post-Tx: –1.7% ($p < 0.05$) vs 0.3% FBG from pre-Tx to post-Tx: 167 ± 68 to 119 ± 34 ($p = 0.009$) vs 153 ± 51 to 156 ± 63, $p = 0.004$ (EOS comparison) Insulin Daily dose reduction <50%: 12.8 vs 7.5% Daily dose reduction ≥50%: 15.4 vs 2.5% Insulin free, on OADs: 5.1 vs 2.5% Free of insulin or OADs: 10.3 vs 0 Absolute change in: Body weight: –1.74 vs –0.58 kg TC: –23.1 vs –2.9 mg/dL ($p = 0.04$) Severe infections requiring hospitalization: 12.8 vs 17.5%
Bruno et al. (1987)[137]	Randomized, double-blind	Insulin treated diabetics requiring steroid treatment	DFZ first f/b PDN (*n* = 5), PDN first f/b DFZ (*n* = 5)	–	After 4 weeks HbA1c (%) change: DFZ: 8.53 ± 1.3 to 8.81 ± 1.19 PDN: 8.53 ± 1.30 to 10.71 ± 1.17 ($p < 0.05$) Body weight (kg) change: DFZ: 75.3 ± 2.2 to 76.8 ± 1.3 PDN: 75.3 ± 2.2 to 74.3 ± 2.2 ($p < 0.01$) Insulin (U/day) requirement: DFZ: 28.5 ± 11.4 to 29.3 ± 11.6 PDN: 28.5 ± 11.4 to 46.3 ± 2.0 ($p < 0.001$)
Ferraris et al. (2007)[138]	Randomized, prospective	Renal transplantation, prepubertal patients	At mean of 2.1 years, switched to DFZ (*n* = 15) vs continued MP (*n* = 16)	3-year follow-up Rejection: 0 vs 1	Height velocity Significant increase with DFZ in 1st year Significant decrease with MP for 2 years Significant reduction in IGF-1 with MP but not DFZ Lean body mass increased in both groups, increase over time greater with DFZ Number of overweights: Increased significantly in MP (9 vs 1) TC: Significant increase in MP and decrease in DFZ HDL-C: Significant increase in DFZ but unchanged in MP LDL-C: Significant decrease in DFZ and significant increase in MP BMD: Significant decrease in lumbar spine and whole body BMD over 3 years in MP group, whereas decrease was seen in DFZ only at 3rd year Glucose/insulin ratio >7: Significantly associated with DFZ at 2 and 3 years

OAD, oral anti-diabetic agent; EOS, end of study; ALP, alkaline phosphatase; AE, adverse event

(absolute change: –5 mg/dL in DFZ and 9 mg/dL in PDN groups), postprandial blood glucose (PPBG) (absolute change: 1 mg/dL in DFZ and 7 mg/dL in PDN groups), total cholesterol (TC) (absolute change: –12 mg/dL in DFZ and 17 mg/dL in PDN groups), and LDL (absolute change: –7 mg/dL in DFZ group and 10.5 mg/dL in PDN groups) also indicated that DFZ is safer than PDN in terms of glycemic and lipid parameters.[133]

Another Indian study in children (2–12 years) with idiopathic nephrotic syndrome who were treated with DFZ (*n* = 12) (2.4 mg/kg/day daily for 6 weeks followed by 1.8 mg/kg/alternate day for

6 weeks) or PDN (n = 13) (2.0 mg/kg/day daily for 6 weeks followed by 1.5 mg/kg/alternate day for 6 weeks). Time to induce remission, remission rate, and relapse rate were all similar in both groups with no significant differences. Change in weight and proportion of children who developed cushingoid features did not differ significantly in the two groups. However, the height gain was significantly lower in PDN than DFZ group (1.44 ± 0.45 vs 2.13 ± 0.50 cm) indicating possible growth retardation.[134]

In a double-blind, randomized controlled trial from Switzerland, patients who underwent kidney transplants were randomized in a dose equivalent manner to PDN (n = 11) or DFZ 6 mg (n = 8) and were followed up over 78 weeks. Rejection episodes occurred in three and two cases in PDN and DFZ groups, respectively. Whole body BMD declined significantly in the PDN group but not in the DFZ group. Lumbar BMD declined significantly in PDN than DFZ group (9.1 ± 1.8 vs 3.0 ± 2.4%) with no difference for the loss of BMD in the hip. This data indicates that DFZ can help slow the decline rate of spinal and hip BMD.[135] Another study in kidney transplant patients assessed the impact of the shift from PDN to DFZ (n = 42) and continuation of PDN (n = 40) in the posttransplant period. Over a mean follow-up of 13 months, there were no episodes of rejection or graft dysfunction. In the conversion (DFZ) group, there was a significant reduction in FBG levels (167 ± 68 to 119 ± 34) compared to the PDN group where levels remained elevated (153 ± 51 to 156 ± 63). A similar trend was evident in HbA1c which reduced significantly in the DFZ group (–1.7%) but not in the PDN group (–0.3%). The requirement for antihyperglycemic medication including insulin was reduced in the posttransplant period. About 10.3% of patients in the DFZ group were free of antihyperglycemic medications. The reduction in glycemia was also accompanied by a significant reduction in TC (–23.1 in DFZ vs –2.9 in the PDN group). Thus, conversion from PDN to DFZ in the posttransplant period is associated with improved glycemia and

Table 11: Key summary of expert consensus statements

Hyperglycemia and DKA:
In people with diabetes, the use of steroids causes hyperglycemia and may precipitate DKA in vulnerable populations
Weight gain:
In people with diabetes, weight gain is expected during steroid therapy and is directly related to the steroid dose and duration of the steroid therapy
Adrenal effects:
In people with diabetes, AI can occur with discontinuation of steroids. AI is not related to the dose or duration of steroids
In people with diabetes, iatrogenic Cushing's syndrome is a possibility that is directly proportional to steroid dose
Dyslipidemia, HTN, and CV risk:
In people with diabetes, steroids may cause or exacerbate HTN and dyslipidemia. The risk of CVDs is increased even at a PEQ dose of <5 mg/day
HF:
In people with diabetes, steroids may precipitate HF and thus consider the mineralocorticoid activity of steroids in such populations
Infections:
In people with diabetes, steroids may increase the risk of bacterial, viral, and fungal infections. Classical features of infections may not be evident in some of the patient populations. Further research is necessary to understand the risk of infections in such populations
Drug interactions:
In people with diabetes, steroids may have drug interactions with some antimicrobials and other medications. A watch for systemic toxicity of steroids is necessary with the concomitant use of certain medications
Wound healing:
In people with diabetes, steroids might delay wound healing. Caution is necessary in people with diabetes with preexisting foot ulcers
Acne:
In people with diabetes, steroids may increase the occurrence of acne, especially with higher dosages and in the presence of risk factors
Myopathy:
In people with diabetes, steroids may increase the risk of myopathy and it may occur early in the course with a higher dosage of steroids
Osteoporosis and bone fractures:
In people with diabetes, steroids increase the risk of osteoporosis even at a PEQ dose of 5 mg or more. Duration of steroids is associated with such risk of osteoporosis and related bone fractures
Avascular necrosis:
In people with diabetes, steroids may increase the occurrence of avascular necrosis of the femur and the risk is probably higher with a higher dose of steroids
Cataract and glaucoma:
In people with diabetes, steroids increase the risk of cataracts and the risk increases with the duration of their use
In people with diabetes, steroids may increase the risk of glaucoma
Complications monitoring:
In people with diabetes, specific monitoring approaches are essential for early detection and treatment of various complications
Complications management:
The complexity brought on by steroids in people with diabetes is enormous and clinical decisions in patient management should be individualized
Steroid equivalence:
The "steroid equivalence" should be considered in routine clinical practice appropriately to avoid underdosing or overdosing when shifting from one steroid to another steroid
Deflazacort is an effective and safe steroid with lesser risks of complications. Given its better safety, it can be considered one of the initial choices for people with diabetes requiring steroids

cholesterol levels.[136] Another randomized study in transplant recipients reported that after a follow-up of 2 years, there was a significant increase in lean body mass in the DFZ group than MP group. In lipid parameters, a significant increase in TC and LDL-C occurred in the MP group whereas they decreased significantly in the DFZ group.[138] In insulin-treated people with diabetes, the use of DFZ in PDN equivalent doses has significantly lower rise of HbA1c at 4 weeks compared to PDN. Insulin requirement was significantly lower in DFZ than PDN group (29.3 vs 47.3 U/day). Thus, for subjects with diabetes treated with insulin, DFZ is a wise choice when glycemic control is necessary.[137] These effects of DFZ in comparison to other steroids are due to its lower lipid solubility because of which the transport of active metabolite 21-desacetyl-DFZ across blood blood–brain barrier is limited leading to lesser HPA axis suppression.[129] Therefore, the steroid equivalence concept is very relevant clinically and can help choose appropriate doses of alternative steroids in clinical situations where it is necessary to shift to a safer steroid like DFZ.

- **Expert consensus:** Deflazacort is an effective and safe steroid with lesser risks of complications. Given its better safety, it can be considered one of the initial choices for people with diabetes requiring steroids.

Conclusion

Diabetes is a complex metabolic disorder with multisystem involvement. The comorbidities or intercurrent illnesses that require short-, intermediate-, or long-term use of steroids pose significant challenges in the clinical management of people with diabetes. The complications induced or aggravated by such steroid use may often be overlooked and become evident only when serious enough to attract the attention of the patient and physician. It is important on the part of treating physicians to be aware of likely possibilities with the use of steroids in people with diabetes. Besides the management of glycemia, a holistic approach considering all possible complications discussed in this paper is necessary to maintain the benefit–risk balance in favor of patients (Table 11). The concept of steroid equivalence needs to be rooted in the clinical practice to take appropriate steroids in a dose-equivalent manner to avoid underdosing or overdosing.

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